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TOWNSEND AND TOWNSEND AND CREW
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO CA 94111-3834

EXAMINER	
SIEW,J	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/020,743	Applicant(s) MACK, DAVID H	
	Examiner Jeffrey Siew	Art Unit 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *18 August 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10, 12-34 & 36-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-10, 12-34 & 36-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☒ Interview Summary (PTO-413) Paper No(s). *14A* .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 U.S.C. § 103

1. I.The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) a patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-5,19-21,23,25-29,36-45,47,48 & 50-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao et al (Gene Vol. 156 pp. 207-213 1995) in view of Seilhamer et al (US6,023,659 Feb. 8, 2000).

Claims 1-5, 20,21 & 23 are drawn to displaying expression levels or compound concentration of two samples on a graph in which the first axis corresponds to expression level of first sample and the second axis is perpendicular to first axis and corresponds to expression level of second sample. A mark is displayed and in response to user's input, information about said selected expressed sequence is displayed.

Claim 19 is drawn to claim 1 with the further limitation of displaying third axis wherein the mark is position relative to expression level of a third sample.

Claim 43 is drawn to claim 25 a computer product with the further limitation of having code displaying third axis wherein the mark is position relative to expression level of a third sample

Claims 25-29,36-42,44 & 45 are drawn to a software product that contains code that displays on first axis expression level or compound in first sample, displays on second axis an expression level or compound in second sample, displays a mark whose position is relative to

first or second axis. Moreover, the code receives a response to user's input, information about said selected expressed sequence is displayed.

Claim 47 is drawn to computer system comprising display, processor and memory for displaying a first axis corresponding to expression level of first axis, code for displaying a first axis corresponding to expression level of first axis, code for displaying a mark, code for receiving a response to user's input and displaying information about said selected expressed sequence and a computer readable storage medium for storing codes.

Claims 48 is drawn to computer system comprising display, processor and memory for displaying a first axis corresponding to a compound concentration, code for displaying a first axis corresponding to compound concentration , code for displaying a mark, code for receiving a response to user's input and displaying information about said selected expressed sequence and a computer readable storage medium for storing codes.

Claim 50 is drawn to claim 1 with the use of aural indication.

Claim 51 is drawn to claim 1 with the added limitation of obtaining an internet based resource.

Claim 52 is drawn to claim 1 with the added limitation of selecting two marks.

Zhao et al teach bioimaging analyzer system to compare the expression profiles of thousands of genes cDNAs) simultaneously . They teach the a high density cDNA filter analysis in which expression profiles of 2505 cloned human brain cDNAs (genes) were monitored (see whole document esp. Abstract). Zhao et al teach that the cDNA probes were sequenced and compared with those in GenBank DNA nucleotide sequence Database by BLASTN program prior to preparing the filter. A quantitative analysis of the filter is performed using Fuji Bioimaging Analyzer ABS2000 System and automated quantification program AutoQuant. The final part is sequence analysis in which each clone is characterized by homology search in the GENBANK nucleotide Sequence Database (see page 208 & Figure 1). They applied the system

for the comparative analysis of expression profile of the human cDNAs in brain. The expression profiles were illustrated on graphs by comparing the their scores from two tissues with Microsoft Excel (Microsoft) on a Macintosh personal computer(see page 210-211 and fig. 3). A mark for each gene is positioned relative to the expression levels in the two different samples. Although the reference is silent to the teaching of processor, memory and display, the personal computer inherently contains a display, microprocessor and memory in the form of RAM, ROM and hard disk. It was well known and commonly practiced in personal computers to use aural indications when using a cursor.

Zhao et al do not specifically teach an input from user and returning information of the selected expressed sequence nor a third axis.

Seilhamer et al teach preparing a relational database for a computer system that contains cDNA sequencing data and corresponding match logs indicating a correlation between presently identified cDNA sequences and previously known sequences. These databases may be organized in a table. They teach that a researcher to search the relational database using keywords or a query and to specify a search on the table to seek out specific information (See all of page 17). They teach that these databases and queries assist the scientist in performing many and various data analysis tasks. The databases may be external such as Genbank which is available at National Library of Medicine or SwissProt site maintained by University of Geneva (see col. 6 lines 6-21).

One of ordinary skill in the art would have been motivated to apply Seilhamer et al's use of database in a computer system to Zhao et al's computer system and method of analyzing expression in samples in order to quickly allow user to gain information on the expressed sequences. Zhao et al states that the sequences for the cDNA probes were determined prior to preparing the filter. It would have been prima facie obvious to one of ordinary skill in the art to incorporate Zhao predetermined sequence information into a Seilhamer et al's database for the

computer in order to allow the practitioner to input a query and easily access to information to assist in various data analysis tasks.

Furthermore, one of ordinary skill in the art would have been motivated to apply Seilhamer et al's use of database in a computer system to Zhao et al's computer system and method of analyzing expression in samples in order to quickly allow user to gain information on the expressed sequences. Zhao et al states that the sequences for the cDNA probes were determined prior to preparing the filter. It would have been prima facie obvious to one of ordinary skill in the art to incorporate Zhao predetermined sequence information into Seilhamer et al's database for the computer in order to allow the practitioner to input a query and easily access to information to assist in various data analysis tasks.

Moreover, one of ordinary skill in the art would have been motivated to implement the Microsoft Excel program in code format to display the expression level in order to analyze various data inputs from various samples on different platforms. A program code provides versatility in allowing dynamic input to be analyzed. It would have been advantageous to implement analysis and display on code so that a large number of different samples would be analyzed especially over time. Moreover, the implementation on code would allow the analysis to be performed across different platforms and even different machines. It would have been prima facie obvious to implement the display of the expression levels through a computer code comprising code in order to analyze and display a constantly changing and new input across different platforms and machines.

Moreover, one of ordinary skill in the art would have been motivated to display the expression level on a computer system containing display, processor and memory in order to analyze various data inputs from various samples. A computer system provides excellent data storage and data manipulation capabilities. It would have been advantageous to implement analysis and display on a computer system so that a large number of different samples would be

analyzed. It would have been prima facie obvious to implement the display of the expression levels on a computer system in order to analyze large amounts of data efficiently.

One of ordinary skill in the art would have been motivated to apply a third axis to Zhao et al display format in order to further compare the expression level in a third sample. It would have been advantageous to use d.. format to compare three samples at the same time so that comparisons would be visually easier to interpret and would be performed simultaneously. It would have been prima facie obvious to apply a third axis to Zhao et al's display format in order to analyze more information at the same time. Moreover, it would have been prima facie obvious for the user to select two or more marks of interest in order to retrieve information on more than one expressed sequence.

3. Claims 6-10,12-18 & 30-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al (WO97/27317 21 July 1997) in view of Zhao et al (Gene Vol. 156 pp. 207-213 1995) in further view of Seilhamer et al (US6,023,659 Feb. 8, 2000)).

Claims 6-10 & 12-18 are drawn to claim 1 in which the expression level of expressed sequence is monitored and plurality of hybridization intensities from pairs of matched and unmatched probes are inputted.

Claims 30-34 are drawn to claim 29 with the added limitation that the code further allows input of plurality of hybridization intensities from pairs of matched and unmatched probes.

Lockhart et al teach a method of detecting nucleic acid abundances or concentrations (e.g. expression levels) between two or more samples (see whole document esp. abstract). They teach the simultaneous monitoring of the expression of a multiplicity of genes using perfect match probe and mismatch probes (see page 5,12,47 & esp. 49-50). They teach that expression

monitoring would be useful for both drug safety and toxicology screenings (see page 230) and monitoring various genes in response to defined stimuli such as drugs (see page 22). They teach that monitoring of gene expression may be performed using a computer system running a software program that includes computer code incorporating analysis of hydridization intensities of the screens(see page 90 & Figure 6-8). They teach a method of comparing expression level using the hybridization intensities between the perfect match and mismatch probes (see page 93-101 & Figure 9-10B). They compare the hybridization intensity difference and ratio of the perfect match and mismatch probes with a threshold. The values NPOS, NNEG and LR are calculated for each pair of probes. The analysis is repeated to calculate the average of the differences. They teach that oligonucleotide pairs that show the greatest differential hybridization between two samples can be identified by sorting the observed hybridization ratio and difference values. Based on identified oligonucleotide pair sequences, a gene can be searched for in sequence databases such as GENBANK (see page 128-9). They also display the results in a graph showing differential expression between samples (see Figures 16-17).

Lockhart et al do not teach presenting expression level information by displaying on a first axis representing the expression level in a first sample, displaying on second axis representing the expression level in the second axis and displaying a mark relative to the two axes. Lockhart does not teach an input from user and returning information of the selected expressed sequence.

Zhao et al teach bioimaging analyzer system to compare the expression profiles of thousands of genes cDNAs) simultaneously . They teach the a high density cDNA filter analysis in which expression profiles of 2505 cloned human brain cDNAs (genes) were monitored (see whole document esp. Abstract). Zhao et al also teaches that the cDNA probes were sequenced and compared with those in GenBank DNA nucleotide sequence Database by BLASTN program prior to preparing the filter. A quantitative analysis of the filter is performed using Fuji

Bioimaging Analyzer BAS2000 System and automated quantification program AutoQuant. The final part is sequence analysis in which each clone is characterized by homology search in the GENBANK nucleotide Sequence Database (see page 208 & Figure 1). They applied the system for the comparative analysis of expression profile of the human cDNAs in brain. The expression profiles were illustrated on graphs by comparing the their scores from two tissues with Microsoft Excel (Microsoft) on a Macintosh personal computer(see page 210-211 and fig. 3). Although the reference is silent to the teaching of processor, memory and display, the personal computer inherently contains a display, microprocessor and memory in the form of RAM, ROM and hard disk.

Seilhamer et al teach preparing a relational database for a computer system that contains cDNA sequencing data and corresponding match logs indicating a correlation between presently identified cDNA sequences and previously known sequences. These databases may be organized in a table. They teach that a researcher to search the relational database using keywords or a query and to specify a search on the table to seek out specific information (See all of page 17). They teach that these databases and queries assist the scientist in performing many and various data analysis tasks. The databases may be external such as Genbank which is available at National Library of Medicine or SwissProt site maintained by University of Geneva (see col. 6 lines 6-21).

One of ordinary skill in the art would have been motivated to display the comparative expression levels of genes as in Zhao et al's to Lockhart et al's analysis technique in order to compare the gene expression between two different samples. Zhao et al's display format allows easy visualization of the many different expressions of genes between two samples. It would have been prima facie obvious to construct a graph with an axis representing the gene expression in one sample and another axis representing the gene expression in a second sample in order to compare the differential gene expression between the different samples.

Moreover, one of ordinary skill in the art would have been motivated to apply Seilhamer et al's use of database in a computer system to Zhao et al's computer system and method of analyzing expression in samples in order to quickly allow user to gain information on the expressed sequences. Zhao et al states that the sequences for the cDNA probes were determined prior to preparing the filter. It would have been prima facie obvious to one of ordinary skill in the art to incorporate Zhao predetermined sequence information into a database for the computer in order to allow the practitioner to easily access to information to assist in various data analysis tasks.

4. Claims 22, 24 & 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao et al in view of Seilhamer et al (US6,023,659 Feb 8, 2000) in further view Beattie (US5,843,767 December 1, 1998).

Claims 22 & 24 are drawn to claim 20 with the added limitation the polymer is a protein.

Claim 46 is drawn to claim 44, a computer product with the added limitation the polymer is a protein.

The teachings and suggestions of Zhao et al and Seilhamer et al are described above.

Zhao et al do not teach the use of protein polymers.

Beattie et al teach the use of protein probes such as antibodies in hybridization array (see whole document).

One of ordinary skill in the art would have been motivated to apply Beattie et al's teaching of using protein probes to Zhao et al's expression display in order to compare the expression level of actual translated protein between two samples. Beattie states that the use of antibodies or ligand receptor binding would be applicable to the study of identifying biomolecules. It was well known and commonly practiced to use these ligand -receptor binding techniques in order to actually identify the stage of gene expression i.e. the translated protein. It

would have been prima facie obvious to use Beattie's protein probes and display the results between two samples using Zhao et al's expression method in order to compare the protein levels which represent the final stage of gene expression.

5. Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao et al (Gene Vol. 156 pp. 207-213 1995) in view of Seilhamer et al (US6,023,659 Feb. 8, 2000) in further view of Rosenberg et al (US6,028,593 Feb 22, 2000).

Claim 49 is drawn to claim 1 with added limitation of using a tactile feedback.

The teachings and suggestions of Zhao et al and Seilhamer et al are described previously.

Rosenberg et al teach a mouse which provides a physical sensation feedback.

One of ordinary skill in the art would have been motivated to apply Rosenberg et al's teaching of force feedback interface device to the combined invention of Zhao et al and Seilhamer et al in order to import physical sensation in the interaction. Rosenberg et al states that interaction on a visual and tactile allows improved interaction with computers (see col.1 lines 24-50). It would have been prima facie obvious to apply Rosenberg et al's force feedback interface device to the combined invention of Zhao et la and Seilhamer et al in order to improve the interaction between the computer and user.

6. During the telephone interview of 2/29/00 applicant stated in response to the 103 rejections over Zhao et al, Zhao et al did not know the sequence of the probes until after hybridization which unlike the instant invention the sequence of the probes were known. However, on page 208 results and discussion part (b) Zhao et al did state the cDNA clones were picked up and sequenced prior to preparation of the high density cDNA filters. Moreover, the claims do not recite a specific limitation that the sequence of the probes is the information retrieved rather information in general such as an identifier. It would have been prima facie

obvious that each hybridized cDNA would have been identified with location and identifier so that upon hybridization the correct plasmid would be identified for further sequencing. Moreover, Zhao does state that clones of interest were sequenced and characterized in Genbank nucleotide sequence base by homology. It would have been prima facie obvious that the information determined by Zhao et al would have been available even after the experiment was performed to be retrieved for reanalysis by user.

Rebuttal

7. The response filed 8/18/00 has been fully considered and deemed not persuasive. The response states that Zhao et al did not know the sequence of probes and thus at the time of graphing Zhao did not know sequence or other characteristics of the cDNA sequences used as probes. On page 208 results and discussion part (b) Zhao et al did state the cDNA clones were picked up and sequenced prior to preparation of the high density cDNA filters. Moreover, the claims do not recite a specific limitation that the sequence of the probes is the information retrieved rather information in general such as an identifier. It would have been prima facie obvious that each hybridized cDNA would have been identified with location identifier as well as sequence information so that upon hybridization the correct plasmid would be identified. Moreover, the claimed method does not recite any limitation of the expression assay being performed immediately before displaying information of the mark. It would have been prima facie obvious that the information determined by Zhao et al method would have been available in the computer to be retrieved for reanalysis by user at a later time.

The response further states that in Zhao et al there is no need to receive user input on a particular mark because Zhao would not know the information beforehand. First of all, as stated in the previous paragraph, information on the probes was known beforehand. Second, a supposed

lack of information would not eliminate the need for further information on the probes. One of ordinary skill in the art would have retrieved additional information on the clones that were preferentially expressed in the examined tissue by identifying the probes that bound to the clones (see abstract).

Moreover, the response states that Seilhammer et al does not display information provided by the mark. The basis of the 103 rejection is on the combination of the references. Zhao et al teach the computer display of marks that represent the different expressed profiles of the cDNA (see Figure 3) while Seilhammer teach the data structures of cDNA information for retrieving in computer system. One of ordinary skill in the art would have been motivated to apply Seilhamer et al's use of database in a computer system to Zhao et al's computer system and method of analyzing expression in samples in order to quickly allow user to gain information on the expressed sequences. It was well known the time of the invention that the state of art of computer systems contained tactile/visual/audio interfaces e.g. mouse, soundblaster cards which enabled user to interact with computer in retrieving information. The rejections are maintained.

SUMMARY

8. No claims allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CONCLUSION

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Siew whose telephone number is (703) 305-3886 and whose e-mail address is Jeffrey.Siew@uspto.gov. The examiner can best be reached on Monday through Thursday from 6:30 a.m. to 4 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist for Technology Center 1600 whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official

Gazette, 1096 OG 30 (November 15, 1989). The CM1 Center numbers for Group 1600 are Voice (703) 308-3290 and Fax (703) 308-4556 or (703) 308-4242.

Jeffrey Siew

October 23, 2000

KENNETH R. HORLICK
PRIMARY EXAMINER
GROUP ~~1800~~ 1600 10/30/00
Kenneth R. Horlick, Ph.D.